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Related Articles, Links

1: J Allergy Clin Immunol. 2003 Mar;111(3):592-7.

ELSEVIER FULL-TEXT ARTICLE

Increased serum cutaneous T cell-attracting chemokine (CCL27) levels in patients with atopic dermatitis and psoriasis vulgaris.

Kakinuma T, Saeki H, Tsunemi Y, Fujita H, Asano N, Mitsui H, Tada Y, Wakugawa M, Watanabe T, Torii H, Komine M, Asahina A, Nakamura K, Tamaki K.

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BACKGROUND: Both atopic dermatitis (AD) and psoriasis vulgaris (PsV) are characterized as chronic and relapsing inflammatory skin diseases associated with various immunologic abnormalities. Cutaneous T cell-attracting chemokine (CTACK; CCL27) is a member of the CC chemokine family and a functional ligand for CC chemokine receptor 10. It is selectively expressed in skin and attracts CC chemokine receptor 10-expressing skin-homing memory T cells. The epidermal keratinocyte is a main source of CTACK, suggesting the involvement of various inflammatory skin diseases. OBJECTIVE: The purpose of this investigation was to clarify whether CTACK produced by keratinocytes is detected in the sera of patients with AD and PsV and to examine the correlation between the serum CTACK levels and disease activity of patients with AD and PsV. METHODS: We measured the serum CTACK levels in 50 patients with AD, 30 patients with PsV, and 22 healthy control subjects. We also divided 50 patients with AD into 3 groups (ie, those with mild, moderate, and severe disease) and compared them among 3 categories. Moreover, we compared the serum CTACK levels of patients with AD and PsV with clinical or laboratory data. Immunohistochemical staining of CTACK and IFN-induced protein of 10 kd (IP-10; CXCL10) was performed on the lesional skin of patients with AD and PsV. RESULTS: The serum CTACK levels in patients with AD and PsV were significantly higher than those in healthy control subjects. The serum CTACK levels in patients with AD significantly correlated with scoring atopic dermatitis (SCORAD) scores, serum soluble IL-2 receptor levels, serum soluble E-selectin levels, serum thymus and activation-regulated chemokine levels, and serum macrophage-derived chemokine levels. Serum CTACK levels in patients with PsV significantly correlated with the serum IP-10 levels but not with the Psoriasis Area and Severity Index score. Immunohistochemical staining showed CTACK was strongly expressed in lesional ke-ratinocytes of patients with AD and PsV, whereas IP-10 was strongly expressed in lesional keratinocytes of patients with PsV and focally in those with AD. CONCLUSION: These results suggest that CTACK might be one of the important chemokines for the pathogenesis of AD and PsV.

PMID: 12642842 [PubMed - indexed for MEDLINE]

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Related Articles, Links

1: Nat Med. 2002 Feb;8(2):157-65.

Comment in:
- Nat Med. 2002 Feb;8(2):117-8.

nature medicine

CCL27-CCR10 interactions regulate T cell-mediated skin inflammation.

Homey B, Alenius H, Muller A, Soto H, Bowman EP, Yuan W, McEvoy L, Lauerma AI, Assmann T, Bunemann E, Lehto M, Wolff H, Yen D, Marxhausen H, To W, Sedgwick J, Ruzicka T, Lehmann P, Zlotnik A.

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The skin-associated chemokine CCL27 (also called CTACK, ALP and ESkine) and its receptor CCR10 (GPR-2) mediate chemotactic responses of skin-homing T cells in vitro. Here we report that most skin-infiltrating lymphocytes in patients suffering from psoriasis, atopic or allergic-contact dermatitis express CCR10. Epidermal basal keratinocytes produced CCL27 protein that bound to extracellular matrix, mediated adhesion and was displayed on the surface of dermal endothelial cells. Tumor necrosis factor-alpha and interleukin-1beta induced CCL27 production whereas the glucocorticosteroid clobetasol propionate suppressed it. Circulating skin-homing CLA+ T cells, dermal microvascular endothelial cells and fibroblasts expressed CCR10 on their cell surface. In vivo, intracutaneous CCL27 injection attracted lymphocytes and, conversely, neutralization of CCL27-CCR10 interactions impaired lymphocyte recruitment to the skin leading to the suppression of allergen-induced skin inflammation. Together, these findings indicate that CCL27-CCR10 interactions have a pivotal role in T cell-mediated skin inflammation.

PMID: 11821900 [PubMed - indexed for MEDLINE]

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1: J Dent Res. 2003 Aug;82(8):621-6.

Differential injury responses in oral mucosal and cutaneous wounds.

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Oral mucosa heals faster than does skin, yet few studies have compared the repair at oral mucosal and cutaneous sites. To determine whether the privileged healing of oral injuries involves a differential inflammatory phase, we compared the inflammatory cell infiltrate and cytokine production in wounds of equivalent size in oral mucosa and skin. Significantly lower levels of macrophage, neutrophil, and T-cell infiltration were observed in oral vs. dermal wounds. RT-PCR analysis of inflammatory cytokine production demonstrated that oral wounds contained significantly less IL-6 and KC than did skin wounds. Similarly, the level of the pro-fibrotic cytokine TGF-b1 was lower in mucosal than in skin wounds. No significant differences between skin and mucosal wounds were observed for the expression of the anti-inflammatory cytokine IL-10 and the TGF-beta1 modulators, fibromodulin and LTBP-1. These findings demonstrate that diminished inflammation is a key feature of the privileged repair of oral mucosa.

PMID: 12885847 [PubMed - indexed for MEDLINE]

A5

CCR10 Expression by Malignant Melanoma Cells: Implications for Tumor Growth and Metastasis

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Malignant Melanoma shows aggressive primary tumor growth and metastasizes into local draining lymph nodes, lung, liver, brain and bone marrow. In contrast to other malignancies, malignant melanoma also shows a high frequency of skin metastases. Recently, we showed that chemokine receptors such as CXCR4 are involved in the development of organ-specific metastasis to lymph nodes and lung. Furthermore, we identified the novel skin-associated chemokine CCL27(CTACK, ALP, ESkine) and its receptor CCR10(GPR-2) which specifically mediate the recruitment of lymphocytes into the skin. In the present study, we demonstrate that malignant melanoma cell lines as well as primary malignant melanoma tumors express high levels of CCR10 mRNA. Notably, skin metastases of malignant melanoma show significantly increased CCR10 mRNA expression compared to primary tumors suggesting the selection for CCR10-high expressing malignant clones. Immunohistochemical analyses confirmed CCR10 expression by MelanA-positive melanoma cells. *In vitro*, CCR10 signaling mediated migration and invasion of malignant melanoma cells and significantly induced their proliferation. *In vivo*, neutralization of mCCL27 resulted in delayed primary tumor growth of human melanoma cells in a SCID mouse model. Taken together, our findings suggest that CCR10 expression by malignant melanoma cells plays a role in primary tumor growth and the development of skin metastases.

MEETING: Investigative Dermatology 2003 Meeting
Fontainbleau Hilton
Miami Beach, Fl.
April 30 - May 4, 2003